

We claim:

1. A microfluidic device comprising:  
a substrate bearing a first electrode and a second electrode spaced a distance  
from said first electrode;  
5 means for passing an individual particle or biological cell in the vicinity of said  
first and second electrodes;  
means electrically connected to said first electrode for selectively applying an  
electrical signal;  
means for detecting signals resulting from the application of the signal to said  
10 first electrode; and  
means for determining a characteristic of said particle or biological cell from  
said detected signal.
2. The device of claim 1 wherein said means for passing an individual particle or  
15 biological cell in the vicinity of said first and second electrodes comprises:  
fluid input means for inputting a fluid comprising a concentration of said particle  
or cell; and  
a channel positioned adjacent said first electrode and said second electrode,  
said channel being coupled to said fluid input means, wherein said particle or  
20 biological cell flows through said channel.
3. The device of claim 2 wherein said channel has a width substantially the same  
as said distance of the spacing between said first electrode and said second  
electrode.
- 25 4. The device of claim 2 wherein said distance of the spacing of said first  
electrode and said second electrode and said width of said channel are  
selected such that in combination with a flow rate a said fluid from said fluid  
input means and said concentration of said biological cell in said fluid, said  
30 biological cells pass one by one through said channel between said first and  
second electrodes.

5. The device of claim 4 wherein said distance is in the range of 1 nm to 1 mm.
6. The device of claim 5 wherein said distance and said width of said channel are in the range of about 10 nm to about 50  $\mu$  m.
- 5 7. The device of claim 6 wherein a height of said channel is in the range of about 10 nm to about 60  $\mu$  m.
8. The device of claim 4 wherein said fluid input means has a flow rate in the  
10 range of about 1 mL/hr to about 300 mL/hr.
9. The device of claim 8 wherein said flow rate is about 1 mL/hr to about 5 mL/hr.
10. The device of claim 2 wherein said fluid input means is a syringe pump.
- 15 11. The device of claim 1 wherein said electrical signal applied to said first electrode is an AC voltage at a predetermined frequency.
12. The device of claim 5 wherein the applied frequency is between about 1 Hz and  
20 about mHz.
13. The device of claim 6 wherein the applied frequency is in the range of about 1 kHz to about 100 GHz.
- 25 14. The device of claim 1 wherein said means for determining a characteristic of said cell comprises measuring impedance of said electrodes.
15. The device of claim wherein said means for determining a characteristic of said cell comprises measuring change in total capacitance.
- 30 16. The device of claim 1 wherein said means for determining a characteristic of said cell comprises measuring capacitance using an AC bridge.

17. The device of claim 1 wherein said biological characteristic of said cell is a DNA content, RNA content or protein content in said cell.
- 5 18. The device of claim 1 wherein said channel is formed on said substrate using a photolithography etch.
19. The device of claim 1 wherein said channel is formed from photolithography.
- 10 20. The device of claim 19 wherein said channel is formed of polydimethylsiloxane.
21. The device of claim 20 wherein said channel is oxidized.
22. The device of claim 21 wherein said channel is oxidized using a de-generated oxygen plasma.
- 15 23. The device of claim 21 further comprising:  
a conductive block for mounting said substrate; and  
a heater mounted to said block, wherein said heater controls the temperature of  
20 said device.
24. A microfluidic device comprising:  
a substrate bearing a first electrode and a second electrode spaced a distance  
from said first electrode;  
25 means for passing a fluid in the vicinity of said first and second electrodes;  
means electrically connected to said first electrode for selectively applying an  
electrical signal;  
means for detecting signals resulting from the application of the signal to said  
first electrode; and  
30 means for determining from the detected signal a characteristic of said fluid.

25. The device of claim 24 wherein said means for passing a fluid in the vicinity of said first and second electrodes comprises:  
fluid input means for inputting a fluid; and  
a channel positioned adjacent said first electrode and said second electrode,  
5 said channel being coupled to said fluid input means, wherein said fluid flows through said channel.
26. The device of claim 24 wherein said channel has a width substantially the same as said distance of the spacing between said first electrode and said second  
10 electrode.
27. The device of claim 26 wherein said distance is in the range of 1 nm to 1 mm.
28. The device of claim 24 wherein said electrical signal applied to said first  
15 electrode is an AC voltage at a predetermined frequency.
29. The device of claim 24 wherein the applied frequency is between about 1 Hz and about 100GHz.
- 20 30. The device of claim 29 wherein the applied frequency is in the range of about 1 kHz to about 100 GHz.
31. The device of claim 24 wherein said means for determining a characteristic of said cell comprises measuring impedance of said electrodes.  
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32. The device of claim 24 wherein said means for determining a characteristic of said cell comprises measuring change in total capacitance.
33. The device of claim 24 wherein said means for determining a characteristic of  
30 said cell comprises measuring capacitance using an AC bridge.

34. The device of claim 24 wherein said channel is formed on said substrate using a photolithography etch.
35. The device of claim 24 wherein said channel is formed from photolithography.
- 5 36. The device of claim 24 wherein said channel is formed of polydimethylsiloxane.
37. The device of claim 24 further comprising:  
a conductive block for mounting said substrate; and  
10 a heater mounted to said block, wherein said heater controls the temperature of said device.
38. The device of claim 24 wherein said fluid is a liquid or aerosol.
39. A nanofluidic device comprising:  
15 a substrate bearing a first electrode and a second electrode spaced a distance from said first electrode to form a first channel;  
a second channel is formed on top of said first electrode and said second electrode;  
means for passing a fluid into said second channel and at least a portion  
20 of said fluid flowing into said first channel in the vicinity of said first and second electrodes;  
means electrically connected to said first electrode for selectively applying an electrical signal;  
means for detecting signals resulting from the application of the signal to  
25 said first electrode; and  
means for determining from the detected signal a characteristic of said fluid.
40. The device of claim 39 wherein said first channel has a width substantially the  
30 same as said distance of the spacing between said first electrode and said second electrode.

41. The device of claim 39 wherein said distance is in the range of 10 nm to 100 nm.
42. The device of claim 41 wherein said second channel has a width in the range of about 1 $\mu$ m to about 100  $\mu$ m.
43. The device of claim 39 wherein said electrical signal applied to said first electrode is an AC voltage at a predetermined frequency.
44. The device of claim 39 wherein the applied frequency is between about 1 Hz and about 100GHz.
45. The device of claim 39 wherein the applied frequency is in the range of about 1 kHz to about 100 GHz.
46. The device of claim 39 wherein said means for determining a characteristic of said cell comprises measuring impedance of said electrodes.
47. The device of claim 39 wherein said means for determining a characteristic of said cell comprises measuring change in total capacitance.
48. The device of claim 39 wherein said means for determining a characteristic of said cell comprises measuring capacitance using an AC bridge.
49. The device of claim 39 wherein said channel is formed on said substrate using a photolithography etch.
50. The device of claim 39 wherein said channel is formed from photolithography.
51. The device of claim 39 wherein said channel is formed of polydimethylsiloxane.
52. The device of claim 39 further comprising:

a conductive block for mounting said substrate; and  
a heater mounted to said block, wherein said heater controls the  
temperature of said device.

5 53. The device of claim 39 wherein said fluid is a liquid or aerosol.

54. A method for measuring DNA content in a biological cell comprising:  
providing a substrate bearing a first electrode and a second electrode  
spaced a distance from said first electrode;  
10 passing an individual biological cell in the vicinity of said first and second  
electrodes;  
applying an electrical signal to said first electrode;  
detecting signals resulting from the application of the signal to said first  
electrode; and  
15 determining a characteristic of said cell from said detected signal.

55. The method of claim 54 wherein said step of passing fluid in the vicinity of said  
first and second electrodes comprises:  
fluid input means inputting a fluid; and  
20 a channel positioned adjacent said first electrode and said second  
electrode, said channel being coupled to said fluid input means, wherein said  
fluid cell flows through said channel.

56. The method of claim 54 wherein said channel has a width substantially the  
25 same as said distance of the spacing between said first electrode and said  
second electrode.

57. The method of claim 54 wherein said distance and said width of said channel  
are in the range of about 10 nm to about 50  $\mu$  m.

30 58. The method of claim 57 wherein a height of said channel is in the range of  
about 10 nm to about 60  $\mu$  m.

59. The method of claim 54 wherein said flow rate is about 1 mL/hr to about 5 mL/hr.
- 5 60. The method of claim 54 wherein said electrical signal applied to said first electrode is an AC voltage at a predetermined frequency.
61. The method of claim 60 wherein the applied frequency is in the range of about 1 kHz to about 10 kHz.
- 10 62. The device of claim 55 wherein said step of determining a characteristic of said cell is accomplished by measuring change in total capacitance.
63. A method for analyzing cell-cycle kinetics in a population of biological cells comprising:
- 15 a) providing a substrate bearing a first electrode and a second electrode spaced a distance from said first electrode;
- b) passing an individual biological cell in the vicinity of said first and second electrodes;
- 20 c) applying an electrical signal to said first electrode;
- d) determining a characteristic capacitance or impedance of said cell from said detected signal,
- e) repeating steps b-d for each cell in the population.
- 25 64. The method of claim 63 further comprising the step of:
- f) analyzing the characteristic capacitance or impedance of the cells in the population.
65. A method of determining the nucleotide sequence of an individual
- 30 polynucleotide molecule comprising differentially labeled nucleotides comprising the steps of:



passing an individual labeled polynucleotide molecule through the  
nonfluidic device of claim 39; and  
detecting the differentially labeled nucleotides.

- 5 66. A method of detecting a malignant cell in a sample population of cells comprising the steps of:  
measuring the DNA content in individual biological cells using the  
method of claim 54;  
10 comparing the DNA content of sample population of cells to the DNA content to a reference population of cells.
67. The method of claim 66 further comprising the step of measuring the DNA content of a reference population of cells using the method of claim 54.
- 15 68. A method of diagnosing a disease state characterized by abnormal cell-cycle kinetics comprising the steps of:  
determining the cell-cycle kinetics of a sample population of cells using the method of claim 63; and  
20 comparing the cell-cycle kinetics of the sample population of cells with the cell-cycle kinetics of a reference population of cells.
69. A method for determining the capacitance of a fluid comprising:  
providing a substrate bearing a first electrode and a second electrode spaced a distance from said first electrode;  
25 passing a fluid in the vicinity of said first and second electrodes;  
applying an electrical signal to said first electrode;  
detecting signals resulting from the application of the signal to said first electrode; and  
30 determining the capacitance of said fluid from said detected signal.
70. A method for determining the capacitance of a particle comprising:

providing a substrate bearing a first electrode and a second electrode spaced a distance from said first electrode;

passing a fluid comprising a particle in the vicinity of said first and second electrodes;

5           applying an electrical signal to said first electrode;

detecting signals resulting from the application of the signal to said first electrode; and

determining the capacitance of said particle from said detected signal.

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